

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Elizabeth M. Denholm, Yong-Qing Lin, and Paul J. Silver

Serial No.: 09/715,965

Art Unit: 1651

Filed: November 17, 2000

Examiner: Meller, M.

For: *ATTENUATION OF TUMOR GROWTH, METASTASIS AND  
ANGIOGENESIS*

Assistant Commissioner for Patents  
Washington, D.C. 20231

**INFORMATION DISCLOSURE STATEMENT**

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit an Information Disclosure Statement, including five (5) pages of Form PTO-1449 and a copy of twenty-six (26) document cited therein, and a copy of the International Search Report mailed June 25, 2001 in PCT/US00/31663, which corresponds to the above-identified application. We were unable to locate copies of those references indicated with an asterisk (\*). We will forward copies of these shortly.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 50-1868.

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### U.S. Patents

<u>Number</u>	<u>Issue Date</u>	<u>Patentee</u>	<u>Class/Subclass</u>
4,696,816	09-29-1987	Brown	424/94
5,567,417	10-22-1996	Sasisekhara et al.	424/94.5
5,945,403	08-31-1999	Folkman et al.	514/21

### Foreign Documents

<u>Number</u>	<u>Publication Date</u>	<u>Patentee</u>	<u>Country</u>
WO 96/01894	01-25-1996	IBEX Technologies	PCT
WO 96/01648	01-25-1996	IBEX Technologies	PCT
WO 96/08559	03-21-1996	Cardiac CRC Nominees PTY, LTD.	

### Publications

CRUM, et al., "A new class of steroids inhibits angiogenesis in the presence of heparin or a heparin fragment," *Science* 230(4732): 1375-1378 (1985).

\*CULP, et al., "Two functionally distinct pools of glycosaminoglycan in the substrate adhesion site of murine cells," *J. Cell Biol.* 79(3):788-801 (1978).

DENHOLM, et al., "The effects of bleomycin on alveolar macrophage growth factor secretion," *Am J Pathol.* 134(2):355-63 (1989).

\*DENHOLM, et al., "Chondroitinase AC inhibits tumor cell invasion, proliferation, and angiogenesis," *FASEB J* 14(4): A702 (2000).

\*DENHOLM, et al., "Anti-tumor activities of chondroitinase AC and chondroitinase B: inhibition of angiogenesis, proliferation and invasion," *Eur J Pharmacol* 416(3): 213-221 (2000).

\*FAASSEN, et. al., "A cell surface chondroitin sulfate proteoglycan, immunologically related to CD44, is involved in type I collagen-mediated melanoma cell motility and invasion," *J. Cell Biol.* 116(2):521-531 (1992).

FAASSEN, et. al., "Cell surface CD44-related chondroitin sulfate proteoglycan is required for transforming growth factor-beta-stimulated mouse melanoma cell motility and invasive behavior on type I collagen," *J. Cell Science* 105(Pt 2):501-511 (1993).

\*FOLKMAN, "Angiogenesis in cancer, vascular, rheumatoid and other disease," *Nat Med* 1(1):27-31 (1995).

FOLKMAN, "Successful treatment of an angiogenic disease," *N. Engl. J. Med.* 320(18): 1211-1212 (1989).

\*FOLKMAN, "Tumor angiogenesis: therapeutic implications," *N. Engl. J. Med.* 285(21): 1182-1186 (1971).

FOLKMAN, et al., "Angiogenesis inhibition and tumor regression caused by heparin or a heparin fragment in the presence of cortisone," *Science* 221(4612): 719-725 (1983).

FOLKMAN, et al., "Control of angiogenesis with synthetic heparin substitutes," *Science* 243(4897): 1490-1493 (1989).

FORRESTER, et al., "A paradigm for restenosis based on cell biology: clues for the development of new preventive therapies," *J. Am. Coll. Cardiol.* 17(3):758-769 (1991).

\*GU, et. al., "Purification, characterization and specificity of chondroitin lyases and glycuronidase from *Flavobacterium heparinum*," *Biochem. J.* 312(Pt 2):569-577 (1995).

HENKE, et. al., "CD44-related chondroitin sulfate proteoglycan, a cell surface receptor implicated with tumor cell invasion, mediates endothelial cell migration on fibrinogen and invasion into a fibrin matrix," *J. Clin. Invest.* 97(11):2541-2552 (1996).

INGBER, et al., "*Inhibition of angiogenesis through modulation of collagen metabolism*," *J. Lab. Invest.* 59: 44-51 (1989).

INGBER, et al., "A possible mechanism for inhibition of angiogenesis by angiostatic steroids: induction of capillary basement membrane dissolution," *Endocrinol.* 119(4): 1768-1775 (1986).

INGBER, et al., "Mechanochemical switching between growth and differentiation during fibroblast growth factor-stimulated angiogenesis in vitro: role of extracellular matrix," *J. Cell. Biol.* 109(1): 317-330 (1989).

JACKSON et. al., "Glycosaminoglycans: molecular properties, protein interactions, and role in physiological processes," *Physiol. Rev.* 71(2):481-530 (1991).

\*JIN-INCHI, et al., "Inhibition of experimental metastasis of murine Lewis lung carcinoma by an inhibitor of glucosylceramide synthase and its possible mechanism of action," *Cancer Res.* 50:6731-6737 (1990).

\*LIDA, et al., "Cell surface chondroitin sulfate proteoglycans in tumor cell adhesion, motility and invasion," *Sem. Cancer Biol.* 7:155-162, (1996).

LINHARDT, et al., "Polysaccharide lyases," *Appl. Biochem. Biotech.* 12(2): 135-176 (1986).

LINN et. al., "Isolation and characterization of two chondroitin lyases from *Bacteroides thetaiotaomicron*," *J. Bacteriol.* 156(2):859-866 (1983).

\*MEYER, et al., "Mechanisms of tumour metastasis," *Eur. J. Cancer* 34(2):214-221 (1998).

MICHELACCI, et al., "Isolation and characterization of an induced chondroitinase ABC from *Flavobacterium heparinum*," *Biochim. Biophys. Acta.* 923(2):291-301 (1987).

MURRAY, et al., "Purification and partial amino acid sequence of a bovine cartilage-derived collagenase inhibitor," *J. Biol. Chem.* 261(9): 4154-4159 (1986).

\*NAKAJIMA, et al., "Heparan sulfate degradation: relation to tumor invasive and metastatic properties of mouse B16 melanoma sublines," *Science* 220(4597):611-613 (1983).

RICHARDSON, et al., "Transient morphological and biochemical alterations of arterial proteoglycan during early wound healing," *Exp. Mol. Pathol.* 58(2):77-95 (1993).

SATO, et al., "Submit structure of Chondroitinase ABC from *Proteus vulgaris*," *Agric. Biol. Chem.* 50:1057-1059 (1986).

TABAS, et al., "Lipoprotein lipase and sphingomyelinase synergistically enhance the association of atherogenic lipoproteins with smooth muscle cells and extracellular matrix. A possible mechanism for low density lipoprotein and lipoprotein(a) retention and macrophage foam cell formation," *J. Biol. Chem.* 268(27):20419-20432 (1993).

\*TAKEUCHI, "Effect of chondroitinases on the growth of solid Ehrlich ascites tumour," *Brit J Cancer* 26(2): 115-119 (1972).

\*TROCHAN, et al., "Evidence of involvement of CD44 in endothelial cell proliferation, migration and angiogenesis in vitro," *Int. J. Cancer* 66:664-668 (1996).

\*VOLPI, "Fast moving and slow moving heparins, dermatan sulfate, and chondroitin sulfate: qualitative and quantitative analysis by agarose-gel electrophoresis," *Carbohydrate Res.* 247:263-278 (1993).

YEO, et al., "Alterations in proteoglycan synthesis common to healing wounds and tumors," *Am. J. Pathol.* 138(6):1437-1450 (1991).

\*ZAWADZKI, et al., "Blockade of metastasis formation by CD44-receptor globulin," *Int. J. Cancer* 75(6):919-924 (1998).

### Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicant is of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Pabst', is written over a horizontal line.

Patrea L. Pabst  
Reg. No. 31,284

Dated: August 1, 2002

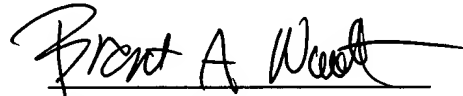
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INFORMATION DISCLOSURE STATEMENT

**Certificate of Mailing under 37 C.F.R. § 1.8(a)**

I hereby certify that this Information Disclosure Statement, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: August 1, 2002

  
Brent A. Winitt

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